



### A Patient Experiencing Anaphylaxis and Urticaria, in Some Cases Preceded by Ingestion of Red Meat

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#### Question:

I am evaluating a 51-year-old woman who lives in South Carolina. She reported 2 episodes of anaphylaxis that developed in the middle of the night and required treatment in the emergency department and several episodes of urticaria. Some of the episodes were preceded by ingestion of red meat 3 to 6 hours before the reactions. The symptoms started 9 months ago.

Regarding the episodes of anaphylaxis, one occurred 6 hours after a meal of eggs with peppers and chicken, and she had no recollection of having red meat. The other episode was preceded by ingestion of red meat.

During the latter episode, she awoke at 3:00 AM with generalized urticaria and was treated with 2 injections of epinephrine and Solu-Medrol. The hives resolved in a few hours. She had eaten beef for dinner at 9 PM that night. None of the episodes were preceded by an insect sting or bite or ingestion of any medications. She had not exercised before either episode.

The patient also reports several episodes of itching, starting on the fingers and then spreading to involve the forearms. Sometimes this is associated with hives. Four of these episodes were preceded by ingestion of beef. Most reactions occur 3 to 6 hours after ingestion of red meat.

She likes to hunt and reports at least 2 tick bites. One tick bite occurred a few years ago and caused a severe reaction, but she cannot remember details, except that she had to go to the hospital for treatment. She also had another tick bite several months ago which caused a large local reaction that persisted for weeks.

She reports that handling shrimp causes swelling, but she tolerates ingestion of cooked shrimp. Nonetheless, she is currently avoiding shrimp and all red meat products and has not been having any episodes of hives, swelling, or anaphylaxis. The episodes of hives were not that frequent even before the change in her diet, so it is hard to say if the dietary elimination is working or not. She never had any problems with dairy, but because of an elevated specific IgE (see below) she is avoiding milk. She is wondering if she will be able to add it back into her diet at some point.

She has been out hunting but reports no further tick bites. In addition, after talking to her some more recently, she reports hand swelling on some occasions in the past, always after doing a lot of dishes. I was thinking of vibratory or some sort of physical angioedema, but she also reports that some of the dishes had red meat on them, and she only had these episodes if she had cuts on her hands. Some of the episodes had associated hives, and one episode progressed to anaphylaxis (which led to an emergency department visit). She had not actually eaten any red meat that day.

Skin tests were negative to beef, pork, and environmental allergens.

Her laboratory results are as follows: IgE beef, 20.7 kU<sub>A</sub>/L; pork, 15.5 kU<sub>A</sub>/L; lamb, 3.08 kU<sub>A</sub>/L; milk, 2.98 kU<sub>A</sub>/L; cat, 4.48 kU<sub>A</sub>/L; dog, 2.75 kU<sub>A</sub>/L; and shrimp, 1.32 kU<sub>A</sub>/L. In addition, her bovine gelatin IgE was <0.35 and alpha-gal was 88 IU/mL.

I have read the articles on alpha-gal allergy but was hoping for some help with the interpretation of these laboratory results. Thanks in advance.

#### Response:

*This query was posed to Scott P. Commins, MD, PhD, Assistant Professor of Medicine and Pediatrics at the University of Virginia Health System, who is one of the leading experts on anaphylactic reactions to "alpha-gal." He responded as follows:*

Thank you for submitting this interesting patient for comment. The patient clearly has a high level of IgE to alpha-gal (an abbreviation for galactose-alpha-1,3-galactose), and the positive laboratory results to mammalian immunoassays are in keeping with the known distribution of alpha-gal. Despite an IgE to alpha-gal of 88 IU/mL, we would not expect positive skin prick tests to mammalian meats. The patient's IgE to shrimp is distinct from the alpha-gal concern, and further evaluation of this sensitization would need to be considered separately. The same can be said of the question of a dairy allergy; her IgE level to cow's milk is low, and you do not give any indication of past reactions to cow's milk, making this allergy seem unlikely but worthy of additional discussion with the patient.

From her history, I suspect that the most recent tick bite has made her more sensitive to mammalian meat and mammalian products, hence the recent reactions. Overall, the described reactions to ingestion sound quite typical in terms of timing (several hours delayed) and severity. A large skin reaction after tick bites that results in intense pruritus and persists for several weeks is frequently reported by patients with IgE to alpha-gal.

The notion that handling meat in preparation for cooking (or cleaning afterward) leads to local reactions is a facet of this syndrome which patients have reported both here at the University of Virginia and to Dr. Heather Gutekunst at Duke University. That is not to say this is commonly reported as an aspect of the allergy in these patients; however, we are aware of 4 to 5 patients who have told us that they do have significant local irritation and even urticaria that can occur after handling, preparing, or washing products that have had meat on them (or liquid from the meat). In most of the patients who have reported symptoms after handling meat, they, like your patient, have noted open sores, cuts, or cracks in the skin of their hands. It is interesting in this case that the local reaction with washing dishes apparently led to a more generalized anaphylactic reaction. To

my knowledge, this has not been reported with IgE to alpha-gal. It is certainly plausible, if there was a large cut or open sore on her hands where mammalian product could enter to create a significant local reaction, that enough resulting mediator release could accumulate, in this unusual instance, to cause anaphylaxis. Perhaps this patient has a predisposing condition (relative deficiency of platelet-activating factor acetylhydrolase) or medication that potentiates allergic responses. Similar to your patient, the reactions that patients have reported to us and Dr. Gutekunst after handling meat have not been delayed, and this seems

consistent with the fact that intradermal skin testing can produce large results in 10 to 15 minutes. The delayed responses after eating mammalian meat are likely due to absorption or processing of the antigen, because it is known from the oncology literature that reactions with intravenous cetuximab infusion occur within minutes.

This being said, I do believe it is reasonable to rule out a vibratory or physical-based cause for these "hand washing" reactions as well. Then there is the issue of IgE to shrimp, and perhaps this has played a role in some of these reactions as well.